

Amendments to the Specification

Please amend the paragraph at page 5, line 24 to page 6, line 6 of the specification as follows:

C¹ wherein n is 0-2; wherein P_X is a phosphorus containing moiety having the structure - P(X)YR_GYR_H, wherein X is independently ~~an alkyl moiety~~ absent, =O or =S; R_G and R_H, for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂ ~~-NR_J-~~, wherein R_J, ~~for each occurrence~~, is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 6, lines 10-17 of the specification as follows:

C² wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂ ~~-NR_J-~~, wherein R_J, ~~for each occurrence~~, is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and wherein M is 1-3.

Please amend the paragraph at page 7, lines 15-21 of the specification as follows:

C³ wherein P_X is a phosphorus containing moiety having the structure -P(X)YR_GYR_H, wherein X is ~~independently an alkyl moiety~~ absent, =O or =S; R_G and R_H, for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent

C3 bond, -O-, -S- or $N(R_J)_2-NR_J-$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 7, line 26 to page 8, line 8 of the specification as follows:

C4 wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J-$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and

Please amend the paragraph at page 15, lines 19-30 of the specification as follows:

C5 "Phosphorus containing moiety" As used herein, the phrase, "phosphorus containing moiety" includes, but is not limited to, phosphonates, bisphosphonates, phosphonic acids, bisphosphonic acids, phosphonic acid amides, tri-substituted phosphines, phosphinoxides, phosphonothionates, phosphoric acids, esters of phosphoric acids to name a few, and substituted versions thereof, to name a few. In certain embodiments of the invention, phosphorus containing moieties include, but are not limited to, phosphorus moieties having the structure $-P(X)YR_GYR_H$, wherein X is ~~independently an alkyl moiety~~ absent, =O, or =S; R_G and R_H , for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J-$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 16, lines 7-19 of the specification as follows:

C6
wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂ -NR_J, wherein R_J, ~~for each occurrence, is independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; V is a halogen; each occurrence of x is independently 1-6, and in certain embodiment is 1-2; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative. It will be appreciated that the compounds of the invention can be substituted with one or more of any of the above-described moieties or any combination thereof. Furthermore, in one subset of compounds, purines are substituted with an aryl or heteroaryl moiety substituted with one or more phosphorus moieties as described above. In certain embodiments, the substituted aryl or heteroaryl moieties are selected from the following:

Please amend the paragraph at page 16, lines 7-19 of the specification as follows:

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wherein each occurrence of M is independently CV, CV₂, -NV-, N, -O- or -S-, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂ -NR_J, wherein R_J, ~~for each occurrence, is independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 0-6; and in certain embodiment is 1-2; wherein L is CW or N, wherein W is hydrogen, aliphatic, heteroaliphatic aryl, alkylaryl, heteroaryl, alkylheteroaryl or hydroxyl; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and

Please amend the paragraph at page 19, lines 23-32 of the specification as follows:

C7 Although it will be appreciated that the compounds of the present invention are intended to encompass structures having a variety of phosphorus containing moieties, in certain embodiments, the one or more phosphorus moieties are each independently a group having the structure $-P(X)YR_GYR_H$, wherein X is ~~independently an alkyl moiety~~ absent, $=O$ or $=S$; R_G and R_H , for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, $-O-$, $-S-$ or $N(R_J)_2$ ~~$-NR_J-$~~ , wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 20, lines 7-15 of the specification as follows:

C8 wherein each occurrence of M is independently CV, CV_2 , $-NV-$, N, $-O-$ or $-S-$, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, $-O-$, $-S-$ or $N(R_J)_2$ ~~$-NR_J-$~~ , wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently an integer from 1-6, and in certain embodiments is 1 or 2; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative or is a combination of the ~~abovedescribed~~ above described moieties.

Please amend the paragraph at page 20, lines 7-15 of the specification as follows:

NE wherein each occurrence of M is independently CV, CV_2 , $-NV-$, N, $-O-$ or $-S-$, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, $-O-$, $-S-$ or $N(R_J)_2$ ~~$-NR_J-$~~ , wherein R_J , ~~for~~

NE
each occurrence, is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 0-6, and in certain embodiments is 1-2; wherein L is N or CW, wherein W is hydrogen, aliphatic, heteroaliphatic, aryl, alkylaryl, heteroaryl, alkylheteroaryl, or hydroxyl; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and

Please amend the paragraph at page 24, lines 17-24 of the specification as follows:

C9
wherein n is 0-2; wherein P_x is a phosphorus containing moiety having the structure - P(X)YR_GYR_H, wherein X is ~~independently an alkyl moiety~~ absent, =O or =S; R_G and R_H, for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is ~~independently~~ a covalent bond, -O-, -S- or N(R_J)₂ -NR_J-, wherein R_J, ~~for each occurrence~~, is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; or is a phosphorus moiety having any one of structures i-viii:

Please amend the paragraph at page 25, lines 7-14 of the specification as follows:

C10
wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂ -NR_J-, wherein R_J, ~~for each occurrence~~, is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivatives; and wherein m is 1-3.

Please amend the paragraph at page 26, lines 20-26 of the specification as follows:

C¹¹ wherein P_X is a phosphorus containing moiety having the structure $-P(X)YR_GYR_H$, wherein X is ~~independently an alkyl moiety~~ absent, $=O$ or $=S$; R_G and R_H , for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, $-O-$, $-S-$ or $N(R_J)_2-NR_J-$, wherein R_J , ~~for each occurrence~~, is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 27, lines 7-14 of the specification as follows:

C¹² wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, $-O-$, $-S-$ or $N(R_J)_2-NR_J-$, wherein R_J , ~~for each occurrence~~, is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and wherein m is 1-3.

Please amend the paragraph at page 39, lines 20-31 of the specification as follows:

C¹³ In certain embodiments, for compounds used in the treatment of cancer, used in inhibiting cellular growth or used in killing cells, either of R_B or R_C is a cyclic or acyclic, substituted or unsubstituted aliphatic or heteroaliphatic moiety, or is an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety substituted with one or more phosphorus moieties, wherein the one or more phosphorus moieties are each independently a group having the structure $-P(X)YR_GYR_H$, wherein X is ~~independently an alkyl moiety~~ absent, $=O$ or $=S$; R_G and R_H , for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic,

C13 heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 40, lines 7-14 of the specification as follows:

C14 wherein each occurrence of M is independently CV, CV₂, -NV-, N, -O- or -S-, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 1-6 or in certain embodiments is 1 or 2; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative.

Please amend the paragraph at page 41, lines 8-16 of the specification as follows:

C15 wherein each occurrence of M is independently CV, CV₂, -NV-, N, -O- or -S-, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 0-6, and in certain embodiments is 1-2; wherein L is CW, wherein W is hydrogen, aliphatic, heteroaliphatic, or hydroxyl; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and

Please amend the paragraph at page 43, lines 9-15 of the specification as follows:

C16 wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂-NR_J, wherein R_J, ~~for each occurrence, is independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative.

Please amend the paragraph at page 45, lines 7-17 of the specification as follows:

C17 In certain embodiments, for compounds used in the treatment of bone disorders, either of R_B or R_C is a cyclic or acyclic, substituted or unsubstituted aliphatic or heteroaliphatic moiety, or is an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety substituted with one or more phosphorus moieties, wherein the one or more phosphorus moieties are each independently a group having the structure -P(X)YR_GYR_H, wherein X is ~~independently an alkyl moiety~~ absent, =O or =S; R_G and R_H, for each occurrence, are independently hydrogen, or substituted or unsubstituted aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, and each occurrence of Y is independently a covalent bond, -O-, -S- or N(R_J)₂-NR_J, wherein R_J, ~~for each occurrence, is independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Please amend the paragraph at page 45, line 23 to page 46, line 6 of the specification as follows:

C18 wherein each occurrence of M is independently CV, CV₂, -NV-, N-, -O- or -S-, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or

C18 N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative.

Please amend the paragraph at page 47, lines 6-14 of the specification as follows:

C19 wherein each occurrence of M is independently CV, CV₂, -NV-, N, -O- or -S-, wherein in structures i, ii, iii, vii, and viii M is not CV or N and in structure iv, v, and vi one M is CV or N, wherein each occurrence of V is independently hydrogen, OH, halogen, or aliphatic; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; each occurrence of x is independently 0-6, and in certain embodiments is 1-2; wherein L is CW, wherein W is hydrogen, aliphatic, heteroaliphatic, or hydroxyl; and each occurrence of R_1 is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative; and

Please amend the paragraph at page 47, lines 6-14 of the specification as follows:

NE wherein each occurrence of M is independently CH, CH₂, CV, CHV, COH, CHOH, or CV₂, wherein in structures i, ii, iii, vii, and viii M is not CH, CV or COH and in structure iv, v, and vi one M is CH, CV or COH; each occurrence of Y is independently a covalent bond, -O-, -S- or $N(R_J)_2-NR_J$, wherein R_J , ~~for each occurrence,~~ is ~~independently~~ hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, or alkylheteroaryl; wherein V is a halogen; each occurrence of x is independently 1-6, and in certain embodiments is 1 or 2; and each occurrence

of R₁ is independently hydrogen, aliphatic, heteroaliphatic, aryl, heteroaryl, alkylaryl, alkylheteroaryl, a prodrug or pharmaceutically acceptable derivative.